Remarks

Claims 2-4, 6-8, 30-42 are pending. Claims 1, 4-5, and 29 have been canceled. Claims 2-3, 6-12, 27-28, 30-31, and 33-36 have been amended.

Claim 2 has been amended to incorporate the limitations found in original claims 3, 29 and 32. Claim 3 is amended accordingly, and claim 29 is canceled. Claims 6-12 have been amended to recite "nucleic acids comprising AAV[2, 3, 4, 5] Rep protein binding sites" instead of AAV[2, 3, 4, 5] inverted terminal repeats, respectively. Support for these amendments can be found on page 9, lines 6-21 of the specification. Therein, Applicants clearly indicate that an ITR is defined by its Rep binding site. Thus, these amendments do not add new matter. Claim 12 is further amended to include the limitations of claim 26. Thus, no new matter is added by this amendment. Claims 27-28, 30-31, 33-36 have been amended to correct dependencies from amended and canceled claims.

Rejection Under 35 U.S.C. § 102

Claim 1 was rejected under 35 U.S.C. § 102(b) as being anticipated by Muster et al. (Virology 35(3):653-61, 1980). To facilitate prosecution, Applicants have canceled claim 1.

Rejection Under 35 U.S.C. § 112, first paragraph

A. Claims 1-42 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The Examiner appears to base the rejection primarily on the position that "the AAV4 capsid protein and its variants as claimed has been defined only by a statement of function that broadly encompasses having any and all characteristics of AAV4, which conveyed no distinguishing information about the identity of the claimed genetic material, such as its relevant structural or physical characteristics." Thus, in order to facilitate prosecution, Applicants have amended claim 2 to incorporate the limitations of claims 29 and 32, reciting 90% homology

instead of 98%, for which support can be found in the specification in the paragraph bridging paragraphs 13 and 14 of the specification.

As the limitations of claim 29 were added to claim 2, claim 29 is canceled herein and claims 30-31 and 33-36 are amended to depend from amended claim 2. These amendments do not present new issues as these limitations were present in the examined claims. Applicants therefore respectfully request that these amendments be entered.

It is believed that this amendment renders moot many of the Examiner's concerns in that AAV4 capsid protein is being limited by structure, i.e., by amino acid sequence. However, the Examiner has also indicated that the variants claimed based on sequence identity failed to meet USPTO written description guidelines for allegedly "fail[ing] to recite any functional limitation associated with structural variants as claimed." Applicants note that prior claim 32 and amended claim 2 recite that the vector system "produces AAV particles." This is clearly a functional limitation that can be assayed by the skilled artisan. Further, it is explicitly taught in the specification (pg. 42, line 17) that it is the differences in capsid proteins that are relevant to the differences in hemagglutination and tissue tropism between AAV4 and other adeno-associated viruses (AAVs). And, at the level of sequence identity claimed (i.e., 90%), the tropism of the variants is expected to be substantially the same as AAV4. In other words, the tropism of the particle produced by the claimed vector system will inherently have AAV4 tropism based on the narrow sequence identity claimed. As such, the reference sequence provided is in fact representative of the genus of particles produced within the claimed scope and is not expected to produce "functionally distinct members." For at least these reasons, the specification clearly provides adequate written description of the claimed variants of AAV4 capsid proteins and vector systems encoding same. The Applicants therefore respectfully request the withdrawal of this rejection as it applies to the amended claims.

B. Claims 1-42 were also rejected under 35 U.S.C. § 112, first paragraph, as not being enabled. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended. Specifically, as indicated above, the claims have been amended such that the

AAV4 capsid protein encoded by the vector system is defined structurally by sequence homology and functionally by the ability to produce AAV particles.

As noted by the Examiner, the test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification, coupled with information known in the art, without undue experimentation. However, one determines undue experimentation not by analyzing a single factor, but rather by analyzing and weighing many factors. The legal standard set out in *In re Forman* 230 U.S.P.Q. 564, 547 (Bd. Pat. App. & Int. 1986) and elucidated in *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400 (Fed. Cir. 1988) sets forth the following factors for consideration: (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples of the invention; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims.

Applicants have provided significant guidance as to the structure and specific function of AAV particles produced by the claimed vector system. The skill in the art of engineering viral vectors is high. And, based on the very high sequence identity claimed for the AAV4 capsid protein (i.e., 90%), there is a high degree of predictability that any given variant produced by the skilled artisan will have the desired characteristics (e.g., tropism). Thus, the variants covered by the amended claims are more likely than not to work in the manner asserted, such that Applicants have shown how to practice the full scope of the currently claimed invention. The Applicants therefore respectfully request the withdrawal of this rejection and allowance of the amended claims.

Pursuant to the above amendments and remarks, reconsideration and allowance of the pending application is believed to be warranted. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.

It is believed that no fee is due with this submission. However, the Commissioner is hereby authorized to charge any fees which may be required to Deposit Account No. 14-0629.

Respectfully submitted,

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P. Brian Giles, Ph.D. — Date: 6-15-07